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*Published in:*  
European Journal of Cancer Care

*DOI:*  
[10.1111/ecc.12806](https://doi.org/10.1111/ecc.12806)


*Publication date:*  
2018

*Document version*  
Publisher's PDF, also known as Version of record

*Document license:*  
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*Citation for published version (APA):*  
Piil, K., Jakobsen, J., Christensen, K. B., Juhler, M., Guetterman, T. C., Fethers, M. D., & Jarden, M. (2018). Needs and preferences among patients with high-grade glioma and their caregivers - A longitudinal mixed methods study. *European Journal of Cancer Care*, 27(2), 1-13. [e12806]. <https://doi.org/10.1111/ecc.12806>

# Needs and preferences among patients with high-grade glioma and their caregivers – A longitudinal mixed methods study

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## Funding information

The study is supported by grants from the Center for Integrated Rehabilitation of Cancer Patients CIRE, established by the Danish Cancer Society and the Novo Nordisk Foundation, from the Neuro Centre at the University Hospital of Copenhagen, the Novo Nordisk Foundation for Clinical Nursing Research, the Capital Regional Research Foundation in Denmark, Torben and Alice Frimodts Foundation, Vera and Flemming Westerbergs Foundation, Hetland Olsen's Foundation and the Research Foundation at the University Hospital of Copenhagen.

Previous reports on the patient perspective of daily life during a 1-year high-grade glioma (HGG) trajectory from the time of diagnosis are sparse. The aim of this longitudinal mixed methods study is to identify the specific needs and preferences for rehabilitation and supportive care and how it links with physical activity, psychological measures and health quality longitudinally over the first year after diagnosis among patients with HGG and their caregivers by integrating qualitative and quantitative findings. Using a longitudinal mixed methods design, patients with malignant glioma ( $n = 30$ ) and their caregivers ( $n = 33$ ) were interviewed and completed questionnaires (patients only) about physical activity level, anxiety/depression and quality of life five times during the 1-year period. Their needs and preferences included interventions designed to re-define hope after diagnosis, health promoting physical activities initiated early, psychological symptom management strategies, and life planning. Caregivers are committed to their caregiving role, but their engagement is nonetheless challenged over time by enormous caregiver burdens. The identified specific needs and preferences favour supportive care, education, information and rehabilitation. Guidelines attentive to these needs and implemented in clinical practice have the potential to improve patients' health-related quality of life and support caregivers by involving them more actively in care and management.

## KEYWORDS

high-grade glioma, needs, preferences, quality of life, supportive care

## 1 | INTRODUCTION

International research continues to contribute to an evidence-based clinical practice for supportive care and rehabilitation in patients diagnosed with high-grade glioma (HGG) (Australian Cancer Network Adult Brain Tumour Guidelines Working Party, 2009; Weller et al., 2014). HGG is a rapidly progressive life-threatening disease with a poor prognosis (Wen & Kesari, 2008) being the most aggressive type of primary brain tumours (Weller et al., 2014). The most common malignant tumor is glioblastoma (45.6%; Louis et al., 2016). The relative survival estimates for glioblastoma are low with a 5% survival rate after 5 years (Ostrom et al., 2014). Standard initial treatment for HGG involves surgery either as diagnostic biopsy or maximal surgical resection. The Stupp regimen including concomitant chemoradiotherapy followed by adjuvant maintenance chemotherapy with temozolomide is currently the standard post-operative treatment (Stupp et al., 2009). Despite this aggressive oncological treatment patients have a limited life span, maintenance of quality of life being an important endpoint (Ownsworth, Hawkes, Steginga, Walker, & Shum, 2009). Unfortunately, quality-of-life in the HGG population and their caregivers remains understudied compared to other groups with a life-threatening cancer diagnosis. A study based upon experiences from patients with lung cancer found that the patients' main concerns include fear of losing independence and being a burden for their relatives (Gralla, Hollen, Msaouel, Davis, & Petersen, 2014). While this also may be of importance for patients with HGG, the situation is far more complicated as brain cancer often leads to cognitive deficits (e.g., personality changes) and physical impairments resulting in the closest relative becoming the caregiver.

Health-related quality of life (HRQOL) has become a particularly important clinical endpoint in the HGG trajectory. The understanding of both the patient and caregiver needs using objective measures of key physical, psychological and HRQOL is imperative for an even more robust understanding of how the situation evolves over time. Survival and HRQOL are negatively influenced by the complexity of symptoms and complications. Impairment of physical condition and fatigue (Giovagnoli, Silvani, Colombo, & Boiardi, 2005; Mauer et al., 2007) lead to severe limitations in daily activities and reduced QOL (Jones et al., 2010). In our previous longitudinal qualitative study we interviewed patients with HGG and their caregivers, and identified a need for information and guidance regarding symptoms and supportive care interventions (Piil, Juhler, Jakobsen, & Jarden, 2015). In the same population we quantitatively measured HRQOL over time and found high levels of anxiety among the newly diagnosed patients (Piil, Jakobsen, Christensen, Juhler, & Jarden, 2015).

This article seeks to expand our understanding of the complexity of the condition for the HGG patients and their caregivers by drawing meta-inferences through the integration of these qualitative and quantitative findings (Fetters, Curry, & Creswell, 2013). Mixed methods (MM) researchers use meta-inferences to understand how combining the findings from the qualitative and quantitative data can add value and provide deeper insight and knowledge (Creswell & Plano Clark, 2011).

Thus, the aim of this longitudinal MM study is to identify the specific needs and preferences for rehabilitation and supportive care and describe its association with physical activity, psychological measures, and health quality longitudinally over the critical first year after diagnosis of HGG for patients and their caregivers by extending beyond the previous quantitative and qualitative analyses, and integrating the qualitative and quantitative findings.

## 2 | MATERIALS AND METHODS

### 2.1 | Study design

In this longitudinal MM study, we collected concurrently qualitative and quantitatively data. Prospectively, the qualitative data were collected individually for patients and caregivers at the same five time-points during their illness trajectory to understand how their experiences with HGG evolved at the time of initial diagnosis, surgery, adjuvant chemotherapy, and post-treatment periods. To describe how the condition evolved quantitative data about anxiety/depression, HRQOL and physical activity level were collected prospectively over a 1-year trajectory from the time of diagnosis. This study is registered by the Danish Data Protection Agency (2007-58-0015/30-0758) and the Ethical Committee at the Capital Region of Denmark (H-2-2013-135) and carried out in accordance with the Declaration of Helsinki.

### 2.2 | Participants and procedures

We recruited subjects consecutively from May to December 2012 at the Department of Neurosurgery, Rigshospitalet University of Copenhagen. The recruited subjects served as the source of the MM sampling for both the qualitative and quantitative data collected at the same five time-points (Creswell, 2015).

The inclusion criteria were participants  $\geq 18$  years of age, newly diagnosed with HGG, functionally able to care for themselves, measured at a Karnofsky performance status  $\geq 60$  and with the ability to speak and understand Danish. Clinical specialists and a neuropsychologist were consulted regarding whether patients with cognitive deficits were able to participate in the study or must be excluded due to severe cognitive deficits. Disease progression was not an exclusion criterion. Adult relatives were eligible if they were named by the patient as the most involved caregiver(s). Patients without relatives could also be included. Patients and their caregivers were recruited on the first postoperative day and provided separate written informed consent within 2 days prior to discharge from the hospital. The principal investigator (KP) recruited the participants and conducted separate interviews with patients and caregivers. Thirty patients and 33 of their caregivers constitute the participants of this study. This sample size was chosen to ensure an adequate number of participants at all five time-points and for the achievement of data saturation. The sample size was based on an expected 50% attrition rate and a median survival time of 12–15 months (Wen & Kesari, 2008).

## 2.3 | Data collection and procedures

### 2.3.1 | Qualitative data collection: semi-structured individual interviews

This longitudinal MM study involved individual telephone interviews with HGG patients and their caregivers at five fixed time-points during a 1-year disease and treatment trajectory (Figure 1). A semi-structured interview guide was applied for each interview (Piil, Jarden, Jakobsen, Christensen, & Juhler, 2013). The intent was to explore the perspectives at critical events (e.g. surgery, treatment and response scans) along the disease and treatment trajectory, starting at the time of diagnosis.

### 2.3.2 | Quantitative data collection: assessment instruments

The results from the *quantitative* data collection regarding physical activity levels, anxiety/depression and HRQOL relied on patient-reported outcomes (PROs) and were collected at the same five time-points as the scheduled interviews (Figure 1). The following instruments were used:

1. Physical Activity—Questionnaire on leisure time physical activity level (Saltin & Grimby, 1968)
2. Anxiety/depression—The Hospital Anxiety and Depression Scale (HADS; Snaith, 2003)
3. HRQOL—The Functional Assessment of Cancer Therapy, General and Brain (FACT-G and FACT-Br; Weitzner et al., 1995)

Patients received the validated questionnaires by mail at the five time-points before their interview with a written instruction explaining how to complete and return the response in an enclosed, addressed envelope. Socio-economic conditions, Karnofsky performance status, disease and treatment variables were obtained from the medical records.

## 2.4 | Data analyses and interpretation

Full details of the analytic procedures for the qualitative findings from the interviews (Piil, Juhler, et al., 2015) and the quantitative results

of the HRQOL questionnaires (Piil, Jakobsen, et al., 2015) have been published previously, but are reviewed succinctly below.

### 2.4.1 | Thematic analysis

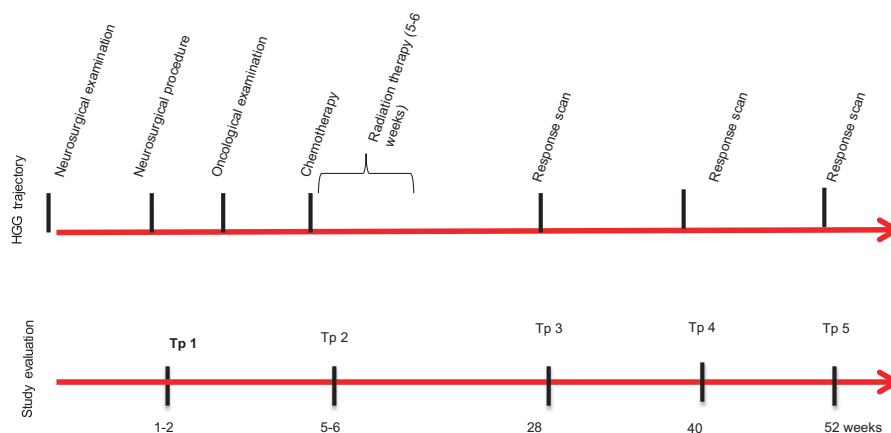
Interview transcripts were imported into the software programme NVivo9 (Skorkjær Binderkrantz & Bøgh Andersen, 2011) to facilitate analysis. Two researchers (KP, MJA) iteratively and reflexively conducted the thematic analysis to ensure trustworthiness and research integrity of the study (Polit & Beck, 2004). The iterative process of the thematic analyses was guided by Braun and Clarke (2014).

### 2.4.2 | Statistical analyses

Responses to the ordinal items of the leisure time physical activity scale, the HADS sub-scales, the FACT-Br sub-scales and the Karnofsky performance status were analysed separately and have been described in detail elsewhere (Piil, Jakobsen, et al., 2015). Participants ( $n = 18$ ) who completed *all* study requirements during the 1-year study period form a subsample allowing for analyses of the differences between *baseline* mean scores (anxiety, depression, FACT-Br sub-scales, FACT Br Trial Outcome Index) and 1-year follow-up assessments, analysed using paired  $t$  tests. The statistical analysis was performed with SAS statistical software, version 9.3.  $p \leq .05$  were considered significant.

### 2.4.3 | Integration of qualitative and quantitative data through use of joint displays to draw meta-inferences

We used a qualitatively framed MM approach for integration (Creswell, 2015). This approach integrates the two datasets. The qualitative findings frame the integration because they provide a window for the development of experiences at the five critical incidents. The quantitative measures provided additional objective details relative to the themes identified by the qualitative data (Onwuegbuzie & Leech, 2005) and expanded the description (Polit & Beck, 2012).



**FIGURE 1** Data collection at five time-points along 1-year high-grade glioma trajectory. HGG: High-grade glioma; TP: Time-point.

A side-by-side joint display facilitated integration through comparison, interpretation, and representation. A joint display is a way to integrate the qualitative and quantitative findings (Guetterman, Fetter, & Creswell, 2015), and has been defined as, "...bringing the data together through a visual means to draw out new insights beyond the information gained from the separate quantitative and qualitative results" (Fetter et al., 2013).

To compare and link the data and in accordance with a qualitatively driven approach, we simultaneously examined the overarching findings of the qualitative interviews and the quantitative results by considering related domains. To build the joint display, the qualitative findings were placed in the first column, and the quantitative findings placed in the second column. The respective qualitative and quantitative findings were moved around within columns to juxtapose related information together in rows. Once, the two types of related data were juxtaposed, we interpreted the findings by looking for commonality between the two data-sets based on the overarching findings of each one. When linked, as part of the qualitatively framed analysis, we then organised the material in an order appropriate for a narrative that could convey the integrated findings. By systematically linking the related findings together, we interpreted the respective meaning and draw meta-inferences, namely, the outcome of interpreting topically related qualitative and quantitative data (Guetterman et al., 2015).

Linking both types of data for interpretation facilitated a theme by construct comparison for drawing overarching conclusions. Based on this juxtaposition, we could then draw conclusions about what the qualitative and the quantitative data were illustrating

both individually and cumulatively (as meta-inferences) about the specific themes. These three elements, the qualitative findings, quantitative findings, and meta-inferences were then included in theme-related tables for results presentation. Merging data in this representation allowed us to look across the two types of data set to look for confirmation, expansion, contradiction or a telling of different ideas (Creswell, 2015).

### 3 | RESULTS

#### 3.1 | Sample

A total of 30 patients comprised the final sample of the study (Figure 2). All patients received radiotherapy and/or chemotherapy. Of 80 potentially eligible patients, 38 were not eligible due to a Karnofsky performance status  $<60$  ( $n = 35$ : aphasia [ $n = 13$ ], severe cognitive impairment [ $n = 9$ ] such as impairments of memory, language and thinking; Meyers & Brown, 2006, severe neurological impairment [ $n = 9$ ] to a degree where inpatient treatment was required, psychotic/severe stress reactions [ $n = 4$ ] requiring acute psychological treatment), and not being able to speak Danish ( $n = 3$ ). Twelve of 42 eligible patients declined participation. A total of 30 patients and 33 caregivers were included. Eighteen patients formed a *sub-sample* as they completed *all* study requirements for the entire study period of 1 year. The response rate for the interviews and the PROs are shown in Tables 1 and 2. Missing data were due to neurological decline or death.

Medical and demographic characteristics of study patients are outlined in Table 3.

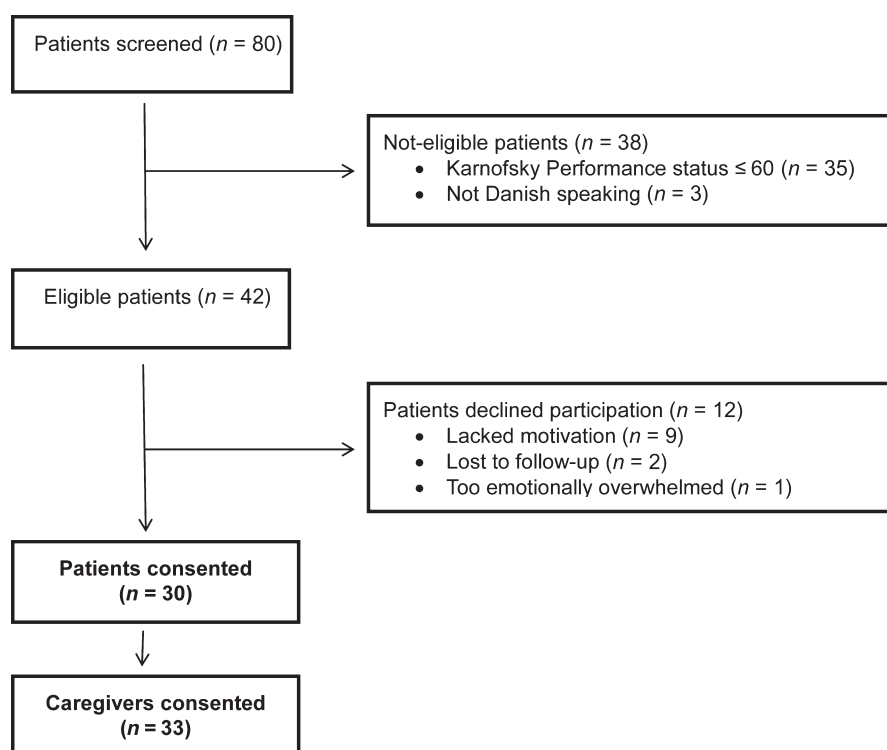


FIGURE 2 Participant enrollment

**TABLE 1** Response rate for the interviews

| Interview time-point        | Patients (average length in minutes) | Caregivers (average length in minutes) |
|-----------------------------|--------------------------------------|--|
| Interview 1                 | 30 (24)                              | 31 (25)                                |
| Interview 2                 | 29 (13)                              | 31 (17)                                |
| Interview 3                 | 27 (16)                              | 30 (20)                                |
| Interview 4                 | 23 (13)                              | 27 (19)                                |
| Interview 5                 | 20 (14)                              | 22 (19)                                |
| Post-bereavement interviews | -                                    | 8 (34)                                 |

Interview 1: baseline; Interview 2: week 6; Interview 3: week 28; Interview 4: week 40; Interview 5: week 52.

**TABLE 2** Response rate for patient-reported outcomes assessment

| PRO assessment Time-point | FACT-Br Number completed (%) | HADS Number completed (%) |
|---------------------------|------------------------------|---------------------------|
| TP 1                      | 28 (93)                      | 28 (93)                   |
| TP 2                      | 29 (97)                      | 29 (97)                   |
| TP 3                      | 28 (93)                      | 26 (87)                   |
| TP 4                      | 21 (70)                      | 21 (70)                   |
| TP 5                      | 18 (60)                      | 18 (60)                   |

FACT-Br: Functional assessment of cancer therapy-brain cancer; HADS: hospital anxiety and depression scale; PRO: patient-reported outcome; time-point 1: baseline; time-point 2: week 6; time-point 3: week 28; time-point 4: week 40; time-point 5: week 52.

### 3.2 | Daily life experiences of patients with HGG and their caregivers

A total of 278 individual semi-structured telephone interviews (length of 13–25 min) with HGG patients ( $n = 30$ ) and their caregivers ( $n = 33$ ) were conducted during a 1-year study period from time of diagnosis. More detailed characteristics of the patients and caregivers are outlined elsewhere (Piil, Juhler, et al., 2015).

Analysis of the interviews identified five main themes (Piil, Juhler, et al., 2015), of which three were shared by both patients and their caregivers, one theme was identified among patients and one among caregivers, only.

1. The first main theme, individual strategy for acquiring prognostic information revealed two different strategies for obtaining additional prognostic information that involved either seeking or limiting the amount and content of prognostic information. At time of diagnosis, it was evident that there were two main strategies regarding prognostic information. However, during the oncological treatments, the strategy of limiting prognostic information became less apparent, but still with the need to oscillate between seeking and limiting strategies depending on individual coping preferences. Patients, however, did gradually gain a higher prognostic awareness.
2. The second theme, described how the patients and their caregivers *shared hope* and that the caregivers have a strong feeling of solidarity with the patient. Hope was expressed in varying ways e.g. through a

positive attitude, putting oneself in a better health care position than others or focusing on concrete projects (further described in theme three). Changes in the expression of hope occurred after tumor progression or symptomatic deterioration as being more orientated towards quality of life than expectation of survival.

3. The third theme *engagement in health promotion activities*, involved the joining forces of patients and caregivers towards a healthier lifestyle. Driven by feelings of hope, a need to become actively involved in health promotion activities reached its peak in the postoperative phase and during the initial phase of the oncological treatment.
4. The fourth theme (patients only), *adjustment to functional limitations* emerged from experiences of and responses to the neurological deterioration resulting in a cognitive and functional decline, limitations of daily activities and role changes. As symptoms progressed, patients adjusted to the neurological decline through an ongoing process of becoming aware, adapting to the loss of functioning, and altering their lifestyle activities.
5. The fifth theme (caregivers only), *role transition from family member to caregiver* described the changing role from being solely a family member to becoming a caregiver. Caregivers were highly engaged in the course of the disease and treatment of the patients. However, the relationship was often challenged by lack of energy and difficulties in managing the patients' limitations, e.g., the cognitive changes.

### 3.3 | Health-related quality of life in patients with a high-grade glioma

Analysis of changes throughout the entire 1-year study period of physical activity levels, Karnofsky performance status, prevalence and severity of anxiety/depression measured by the HADS and HRQOL as measured by the FACT-Br scores was performed in a sub-sample group of patients ( $n = 18$ ) who completed *all* study requirements for the entire study period and presented below. Analyses relying on the primary sample of 30 patients are described elsewhere (Piil, Jakobsen, et al., 2015).

#### 3.3.1 | Physical activity and functional status

Physical activity decreased over time, 89% of the patients being active less than 3 hr/week. All patients had a Karnofsky performance

**TABLE 3** Medical and demographic characteristics for study participants

|   | Patients<br>(n = 30) | Caregivers<br>(n = 33) |
|---|----------------------|------------------------|
| Gender  |                      |                        |
| Male/female   | 19/11                | 10/23                  |
| Age, median (range)   | 57.9 (29–79)         | 50 (29–72)             |
| Diagnosis   |                      |                        |
| Glioblastoma Multiforme (GBM) WHO Grade IV                                | 23                   |                        |
| Primitive Neuroectodermal Tumor (PNET) WHO Grade IV                       | 1                    |                        |
| Gliosarcoma WHO Grade IV  | 1                    |                        |
| Anaplastic Astrocytoma WHO Grade III                                      | 4                    |                        |
| Anaplastic Oligodendroglioma WHO Grade III                                | 1                    |                        |
| Surgical procedure  |                      |                        |
| Operation/biopsy  | 23/7                 |                        |
| Unifocal/multifocal   | 18/12                |                        |
| Marital status  |                      |                        |
| Married/living with partner   | 24                   |                        |
| Single/divorced/living alone  | 6                    |                        |
| Children living at home   | 6                    |                        |
| Highest level of education  |                      |                        |
| Less than or completed municipal primary/9th or 10th class                | 6                    |                        |
| Training/learning   | 13                   |                        |
| Higher education ( $\leq 4$ years)  | 6                    |                        |
| Prolonged higher education ( $\geq 5$ years)                              | 5                    |                        |
| Employment status before diagnosis  |                      |                        |
| Full time   | 19                   | 19                     |
| Part time   |                      | 3                      |
| Sick leave, flex job/student  | 1/0                  | 0/3                    |
| Not employed/early retirement & pension                                   | 0/10                 | 3/5                    |
| Employment status after diagnosis   |                      |                        |
| Full time/part time   | 2/4                  |                        |
| Sick leave  | 14                   |                        |
| Early retirement/pension  | 10                   |                        |
| Changed conditions relating to caregiver responsibilities after diagnosis |                      | 15                     |
| Caring status   |                      |                        |
| Caring for dependent children   |                      | 6                      |
| Not caring for anyone else  |                      | 27                     |
| Relationship with patient   |                      |                        |
| Spouse/partner  |                      | 25                     |
| Child/sibling   |                      | 7/1                    |

status  $\geq 70$  at the first two time-points, and 78% of the patients still had a Karnofsky performance status  $\geq 70$  at the end of the study.

### 3.3.2 | Anxiety and depression

There was an improvement of mean anxiety from time-point 1 to time-point 5 ( $p = .0095$ ). No significant change in depression scores from time-point 1 to time-point 5 was identified ( $p = .07$ ).

### 3.3.3 | Quality of Life

The emotional well-being (EWB) subscale of the FACT-Br improved significantly ( $p = .0023$ ) from baseline ( $13.8 \pm 6.7$ ) to time-point 5 ( $18.4 \pm 4.5$ ; Piil, Jakobsen, et al., 2015). No significant changes were identified for the other subscales. However, according to the social well-being (SWB) sub-scale the patients scored higher at all time-points compared to the normative US values.

The longitudinal MM data are shown in Table 4.



**TABLE 4** Longitudinal mixed methods data and meta-inferences at five time-points

| Time | Critical event type                    | Quantitative results (patients only) |  |  | Qualitative findings   |  |   |
|------|--|--------------------------------------|--|--|--|--|---|
|      |  | HADS                                 | HRQOL                                  | Physical activity and KPS                              | Shared patient and caregiver issues  | Either patient or caregiver issues   | Meta-inferences   |
| TP 1 | Neurosurgery (biopsy or operation)     | High level of anxiety                | Close relation between EWB and anxiety | KPS and level of physical activity decreased over time | Distressed due to the poor prognosis and an unpredictable future<br>Individual strategies for acquiring prognostic information   | Highly engaged in the course of the disease and treatment of the patients (caregivers) | Distress and seeking control as early responses to HGG diagnosis      |
| TP 2 | Oncological treatments                 | Continuous risk of depression        |  | Varying periods of disease stability                   | Need for information related to the HGG trajectory and treatment options<br>A wish to exchange experiences with peers  | Ongoing role transition from family member to caregiver (caregivers)                   | Being pro-active and receiving social support are valuable for EWB    |
| TP 3 | Response scan and treatment evaluation |                                      | High SWB at all test time points       | Activity restriction                                   | Engagement in health promotion activities, patients ended utilisation of CAT (during symptom progression)<br>Shared hope in the beginning and later a need for redefining hope |  | Hope is essential for HRQOL   |
| TP 4 | Response scan and treatment evaluation |                                      |  |  | Searching worldwide for advice and experimental trials   |  | Caregivers capacity and commitment are challenged                     |
| TP 5 | Response scan and treatment evaluation |                                      | EWB improved over time                 | One-year survivors have highest KPS                    | Altered priorities   | Adjustment to functional limitations (patients)  | Patient experience symptom progression and neurological deterioration |

CAT: complementary and alternate therapy; EWB: emotional well-being; HADS: The Hospital Anxiety and Depression Scale; HGG: high-grade glioma; HRQOL: health-related quality of life; KPS: Karnofsky performance status; SWB: social well-being; TP: time-point.

The meta-inferences of the two datasets are represented in the MM visual joint display (Table 5).

## 4 | DISCUSSION OF INTEGRATED RESULTS

This discussion compares and examines the qualitative and quantitative components to evaluate whether the findings are complementary, contradictory or otherwise linked (Table 5).

### 4.1 | Distress and control as early responses to diagnosis of high-grade glioma

Patients and caregivers explained that they were distressed due to the poor prognosis and an unpredictable future. The PROs confirmed this narrative as a high level of anxiety among patients was found at the time of diagnosis. The need of patients and caregivers

for information at this early stage is mainly related to the HGG trajectory and treatment options. A wish to exchange experiences with other patients and/or caregivers was expressed. As a response to this critical stage of the trajectory, both patients and caregivers followed individual strategies for acquiring prognostic information. Moreover, they needed prognostic information to be provided with empathy and in an amount, content and pace that allowed effective assimilation.

Individual strategies for acquiring prognostic information functioned as a tool for the study participants to integrate and understand the reality. No standard approach for measurement of prognostic awareness currently exists (Applebaum et al., 2014). Patients, however, did gradually gain a higher prognostic awareness. This is supported by literature identifying that prognostic awareness can be achieved through interactions with skilled professionals (Jackson et al., 2013). Our data indicate that whether early prognostic awareness is a prerequisite for successful coping and for HRQOL depends on individual



**TABLE 5** Overarching meta-inferences for the 1-year illness trajectory

| Study findings from QUAL component (interviews)  | Meta-inferences   | Study results from quan component (PROs)  |
|--|---|---|
| <p style="text-align: center;"><b>Overall research aim</b></p> <p style="text-align: center;">To identify the specific needs and preferences for rehabilitation and supportive care and how it links with physical activity, psychological measures and health quality longitudinally over the critical first year after diagnosis among patients with HGG and their caregivers by integrating qualitative and quantitative findings</p> |   |   |
| Individual strategy for acquiring prognostic information   | <b><i>Distress and seeking control were early responses to HGG diagnosis.</i></b><br>High level of distress was confirmed by qualitative and quantitative components at an early stage; individual strategies for acquiring PI aided in understanding and adapting to the situation reality   | ↓ Anxiety from TP 1 to TP 5 for 1-year survivors ( $p = .0095$ )<br>Close correlation between EWB and anxiety |
| Shared hope and strong feelings of solidarity  | <b><i>Being pro-active and receiving social support are both valuable for emotional well-being.</i></b><br>Patients and their caregivers joined forces in managing the HGG prognosis together, supported by friends/family; they were actively involved in ways to optimize the therapeutic effect of standard oncological treatments and to improve survival: this engagement may be related to the significant increase in EWB among patients | ↑ EWB for 1-year survivors ( $p = .0023$ )<br>HGG 1-year survivors have highest KPS                           |
| Engagement in health promotion activities  | <b><i>Hope is essential for HRQOL.</i></b><br>Awareness of the life-threatening disease resulted in a shared hope between the patient and the caregiver; some patients and caregivers succeeded with mutual help to redefine hope, shifting focus from survival to HRQOL issues; 12-month survivors ( $n = 18$ ) had higher KPS throughout the study compared to the primary sample, which could explain the increase in EWB ( $n = 18$ )       | Continuous risk of depression (ns change)   |
| Adjustment to functional limitations   | <b><i>Symptom progression and neurological deterioration.</i></b><br>Patients experienced varying periods with stable disease with no or few symptoms and/or complications; symptoms, however, eventually increased in number and severity, often resulting in rapid neurological deterioration (↓ KPS); patients adjusted to the neurological disorders in an ongoing process of becoming aware of and adapting to the loss of function        | ↓ KPS and level of physical activity decreased over time  |
| Role transition from family member to caregiver  | <b><i>Caregivers' capacity and commitment</i></b><br>Caregivers possess a significant capacity to be engaged in the care and support of the patient; however, their commitment is challenged by an enormous caregiver burden; caregivers preferred encouragement from professionals who, for example, acknowledged them an essential contributor to the patients' well-being  | SWB ( $n = 30$ ) at all TP higher than normative value ( $p < .0001$ for baseline to TP5)                     |

CAT: complementary and alternative therapy; EWB: emotional well-being; HGG: high-grade glioma; HRQOL: health-related quality of life; KPS: Karnofsky performance status; ns: not significant; PA: prognostic awareness; PI: prognostic information; PROs: patient-reported outcomes; SWB: social well-being; TP: time point; QUAL: qualitative, use of upper (dominant status) and lowercase letters designates priority; quan: quantitative, lowercase designates the supplementary component.

preferences. Prognostic awareness enables medical decision-making, which might be a motivation for obtaining prognostic information. In this way, acquired prognostic information strategies can be compared with coping, as described in the literature as a healthy, paced integration of information (Jackson et al., 2013). This is supported by a preference for being able to live a normal everyday life for as long as possible by participating in everyday activities.

The qualitative findings show that patients become more interested in greater amounts of prognostic information as time passes which is consistent with the quantitative results suggesting that patients gradually succeed in reducing levels of anxiety. Easy access to brain cancer specialists facilitates this process, and more individually tailored information and an introduction to palliative care teams are recommended (Temel et al., 2010).

## 4.2 | A proactive attitude and social support improve emotional well-being

During oncological treatment, patients and their caregivers described how they joined forces in fighting the HGG prognosis together, supported by friends and family. An imminent need to be actively involved in ways to optimise the therapeutic effect of the standard oncological treatments and to improve survival was identified. A lack of professional support and information about complementary and alternative therapies meant that some patients and caregivers searched worldwide for advice and experimental trials.

Concerns have been raised that a lack of knowledge about complementary and alternative therapies undermines the ability of professionals to communicate the risks and benefits of complementary

**TABLE 6** Needs and preferences of patients with HGG and their caregivers

| Patient needs and preferences  | Patient and caregiver needs and preferences in common  | Caregiver needs and preferences  |
|--|--|--|
| <b>Supportive care needs</b>   |  |  |
| <ul style="list-style-type: none"> <li>• Screening for depression throughout the trajectory</li> <li>• Assistance and help from relatives and health care professionals</li> </ul>   | <ul style="list-style-type: none"> <li>• Anxiety reducing interventions at time of diagnosis</li> <li>• Optimisation of the patients situation through health promoting activities</li> <li>• Help to obtain, maintain or redefine hope and to discuss hope with professionals</li> <li>• Practical help and support from family and friends</li> <li>• Exchange of experiences with other patients and/or caregivers</li> <li>• Living a normal everyday life for as long as possible by participating in everyday activities</li> <li>• Receipt of mutual support between patients and caregivers</li> </ul>   | <ul style="list-style-type: none"> <li>• Supportive care interventions tailored to individual psychosocial needs</li> <li>• Easing of their burden by family and friends (practically, emotionally, socially)</li> <li>• Help and information to manage new responsibilities (e.g. financial, social and care)</li> <li>• Encouragement from professionals who acknowledged them as an essential resource</li> </ul> |
| <b>Educational and information needs</b>   |  |  |
|  | <ul style="list-style-type: none"> <li>• Information about the likely HGG trajectory and treatment options</li> <li>• Individual assistance with how to manage functional and daily adjustments</li> <li>• Information and discussions about health promotion activities and complementary and alternate therapy</li> <li>• Delivery of PI with empathy and at a pace that allows effective assimilation</li> <li>• Improved access to brain cancer specialists throughout the HGG trajectory</li> <li>• Individually tailored information, including introduction to palliative care teams</li> <li>• Easy access to information and specialists in brain cancer</li> <li>• Respect shown toward their chosen strategies for acquiring PI</li> <li>• Education in strategies for life planning</li> </ul> | <ul style="list-style-type: none"> <li>• Information about how to manage brain cancer-related problems and symptoms, e.g. an introduction to the health care system</li> </ul>   |
| <b>Rehabilitation needs</b>  |  |  |
| <ul style="list-style-type: none"> <li>• Interventions focusing on cognitive and physical function</li> <li>• Rehabilitative programmes to target cognitive ability to participate activity</li> <li>• Being as independent as possible for as long as possible</li> <li>• Attending local training programmes due to transportation issues and social needs</li> <li>• Exercising with friends or other patients with similar challenges</li> </ul> |  |  |

HGG: high-grade glioma; PI: prognostic information.

and alternative therapies (Chang & Chang, 2015). Similar to previous studies (Halkett et al., 2015; Janda et al., 2007) the SWB score was higher than the normative values at all time-points, supporting that the expressed feeling of solidarity between patients and caregivers is valuable. Moreover, being pro-active and involved is described in the interviews as being related to well-being and may affect the EWB of the patients positively, explaining the significant increase in the EWB ( $p = .0023$ ) at 1-year. This is supported by the literature that identifies healthier lifestyle changes as a key component of taking control (Lovely et al., 2013). Some of the ways our study participants achieved this was by incorporating new dietary plans with healthy eating habits, reducing smoking and alcohol consumption, using complementary and

alternative therapies and by trying to be more physically active. Finally, a change in the individual's self-evaluation or altered priorities (Adams et al., 2005) could be connected with the increase in EWB. A *declared wish* for a high level of physical activity was in contrast with the patients' PROs on level of physical activity and the measured functional performance that decreased over time.

#### 4.3 | Hope is essential for health-related quality of life

The awareness that HGG is a life-threatening disease resulted in distress and a mutual facilitation of shared hope between the patient

and the caregiver. Patients and caregivers were hopeful that their situation would turn out better than the survival statistics. This study confirms that hope is a source of strength that helps individuals to keep going (Coolbrandt et al., 2015; Sterckx et al., 2015), brings purpose and meaning to life, encourages a positive attitude and improves psychological well-being (Sutton, 2013). However, both patients and caregivers said that they had an *unmet need* to be supported by professionals concerning hope, which was rarely discussed with professionals despite its vital importance for HRQOL (Clayton et al., 2008).

Some patients and caregivers succeeded with mutual help to *re-define hope*, shifting focus from survival to HRQOL issues. According to Cella et al., hope is embedded in the EWB subscale of FACT-Br (Weitzner et al., 1995), whereas, interestingly, the sub-sample analysis ( $n = 18$ ) identified a significant increase ( $p = .0023$ ) in the EWB after 1 year. This result could be explained by the fact that patients who were survivors at 12 months were more hopeful than those who filled out FACT-Br shortly before their death. If hope diminishes, however, it might increase the risk of depression. EWB also has a positive correlation with the level of functional status (Rooney et al., 2013).

The 12-month survivors ( $n = 18$ ) had higher performance status compared to the primary sample ( $n = 30$ ) throughout the study, which could be the reason for the increase in the EWB. Furthermore, the self-reported level of anxiety of patients decreased over time, with correlations to EWB, possibly indicating that they gained value from the shared hope and strong feeling of connection they had together.

#### 4.4 | Symptom progression and neurological deterioration

Patients experienced varying periods of disease stability with no or few symptoms and/or complications during the trajectory. Symptoms, however, eventually increased in number and severity, often resulting in rapid neurological deterioration. Brain cancer related symptoms expressed as fatigue and quantitatively measured in a decreasing performance status caused activity restrictions not only in social relations but also in working life, daily activities and in level of physical exercise.

Maintaining independence for as long as possible was a priority. Patients adjusted to the neurological disorders in an ongoing process of becoming aware of and adapting to loss of functioning. They experienced trouble in understanding and following instruction(s), difficulties in coordinating movements and/or unpleasant symptoms when attending general rehabilitation programmes. They preferred to exercise at their local facilities as it was convenient and fulfilled certain social needs.

Depression has been identified as being part of a symptom cluster (Fox, Lyon, & Farace, 2007). Furthermore, impairment of physical condition and fatigue (Taphoorn et al., 2005) have been found to cause severe limitations in daily activities and reduce QOL (Jones et al., 2010) followed by distressful emotional and psychological reactions such as depression (Boele, Klein, Reijneveld, Verdonck-de Leeuw, & Heimans, 2014; Molassiotis et al., 2010). Finally, brain tumour histology and grade of malignancy affect the production and release of biological factors that cause depressive symptoms (Starkweather et al., 2011), patients being at risk for unrecognised and untreated depression.

In contrast, our sub-group analysis ( $n = 18$ ) identified a decreasing tendency for depression over time (not significant,  $p = .07$ ). This indication is supported by studies identifying patients with HGG that report an acceptable QOL during oncological treatments (Lucchiari et al., 2015). Still, moderate cases of depression are identified at each time-point. Moreover, depressive symptoms according to HADS do not necessarily reflect a clinical depression. It may be difficult, in clinical practice, to distinguish between “understandable” sadness (Singer et al., 2011) and vegetative symptoms of depression, such as loss of interest, emotion and energy as there are not systematically using measurements tools (Weitzner, 1999). Clinical guidelines for diagnosing depression in patients with a glioma have been suggested (Rooney, Brown, Reijneveld, & Grant, 2014).

To manage the symptoms and changes, patients need assistance from their relatives, their closest relation becoming their closest caregiver. Consequently, providing the patients and caregivers with information about symptom management via readily available specialists is recommended. During symptom progression, patients ended their utilisation of complementary and alternate therapy, explaining that it had doubtful effects, was too expensive and time consuming.

#### 4.5 | Caregivers' capacity and commitment

The present study shows that the caregivers possess a significant capacity to be engaged in the care and support of the patient with HGG. As confirmed in the literature (Hrick et al., 2011; Sherwood et al., 2006), commitment to the role of caregiver is nonetheless challenged by an enormous caregiver burden, which in many ways is similar to the experience of caregivers to patients with Alzheimer's disease (Clare, 2003). As the patients' symptoms put a strain on the caregivers' energy level and social relationships, they need support tailored to their individual psychosocial needs, e.g., practical assistance, emotional support, financial information, household tasks and caring tasks (new responsibilities). The patients rely on their family members' ability to support them, and information on how to navigate in the health care system is necessary knowledge for caregivers. Moreover, caregivers preferred encouragement from professionals as they often acknowledged them as essential contributors to the patients' well-being.

#### 4.6 | Needs and preferences

An overview of the needs and preferences extracted from the meta-inferences is presented in Table 6. The present study identified that needs change dynamically along the 1-year process of the HGG trajectory depending on the state of disease and individual preferences rather than a specific time-point. Patients and caregivers share certain needs, e.g., psychosocial needs. However, separate needs were also identified such as patients' needs for symptom management and rehabilitation, while caregivers need support in managing the changed life situation including their new responsibilities. Needs and preferences are outlined according to supportive care, education and information and rehabilitation.

The methodological *strengths* of this study include its *longitudinal design* identifying the changing life situation, needs and preferences of

patients with HGG and their caregivers. The MM design allowing complementary but different methodological tools to provide multiple perspectives on the overall research aim also enhances validity (Bishop & Holmes, 2013; Polit & Beck, 2004). A further advantage is the *serial interviewing with a homogeneous patient sample and their caregivers*, which adds knowledge about the life situation of the *specific* HGG population as well about the relationship between the patients and their caregivers (Kendall et al., 2009). Guidelines for critiquing MM studies have been followed (Polit & Beck, 2012) and the MM approach is believed to have strengthened the conclusions. For example, before MM integration we knew that patients said they were distressed after being diagnosed and found support from their informal caregivers, and now this is confirmed for the quantitative measurements of anxiety that decreased from time of diagnosis, SWB is scored high and EWB that increased over time.

*Limitations* of this study include a small sample size for the *quantitative* component. The subsample ( $n = 18$ ) represent survivors and most likely are not necessarily representative for the patient population, and therefore results should be interpreted with caution. Extensive qualitative data were gathered from study participants representing various demographic characteristics (gender and age). However, patients who declined participation ( $n = 12$ ) might have had experiences that could have expanded these findings. Cognitive impairments frequently occur in patients with HGG. No study participants were excluded once enrolled. Those subjects with the most severe symptoms, emotional status or social support may have been the most likely ones to decline or drop out during the study period. This could bias the findings towards the most physically, emotionally, and socially healthy participants. While it is plausible that for those with an even more serious situation to be similar, the factors noted here may be significantly more rapidly occurring and worse in magnitude. Consequently, care should be taken not to extrapolate these findings to all HGG patients and caregivers without caution. Nonetheless, these findings do represent the perspectives of our participants the longitudinal data collection allowing for a comprehensive assessment.

## 5 | CONCLUSIONS AND CLINICAL IMPLICATIONS

The present findings provide a comprehensive understanding regarding needs and preferences of the patients and caregivers for rehabilitation and supportive care during a 1-year HGG trajectory. Patients and caregivers share some needs but individual and different needs were identified, indicating that the HGG trajectory is a dynamic process experienced differently by patients and caregivers. The needs and preferences among patients and caregivers include interventions aimed to maintain hope after diagnosis, early initiated health promotion activities, strategies for symptom management and life planning. Patients and caregivers shared a similar need for empathy during patient education, wishing to receive information at a pace that would allow effective assimilation.

Symptoms increase in number and severity over time, often resulting in rapid neurological deterioration. However, patients also experience periods of disease stability. Patients are at risk for unrecognised depression throughout the trajectory, because functional limitations and tumour progression are related to prevalence of depression. Maintaining independence is a main priority of the patients, rehabilitative programs targeting the cognitive ability should help the patient to participate actively in everyday life. Following improvement of anxiety, EWB develops during the 1-year trajectory. Interventions aimed to decrease the anxiety are important including social support, physical independence and optimisation of the life situation. Caregivers have a unique commitment to assist the patient and wish to be acknowledged, involved and encouraged for their contribution by health care professionals.

This study supports health care professionals in understanding the impact of a HGG diagnosis on daily life in patients and their caregivers during a 1-year disease and treatment trajectory. Our findings contribute to the existing knowledge about the needs and preferences of the patients and caregivers and should be incorporated into future clinical guidelines for rehabilitation and supportive care. Guidelines implemented in clinical practice have the potential to improve HRQOL of the patients and support caregivers by involving them more actively in care and management. Health care professionals are enabled to take appropriate measures to meet these needs and preferences by taking into consideration the early and late psychosocial needs and individual preferences for prognostic information. Furthermore, incorporating communication about hope and discussions regarding health promoting strategies might well improve the quality of care and facilitate the decision-making and involvement of the patient in treatment, symptom management and life planning.

## CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

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**How to cite this article:** Piil K, Jakobsen J, Christensen KB, et al. Needs and preferences among patients with high-grade glioma and their caregivers – A longitudinal mixed methods study. *Eur J Cancer Care*. 2018;27:e12806. <https://doi.org/10.1111/ecc.12806>